Multidimensional State-Spaces for fMRI and PET Activation Studies

S.C. Strother[1,2], N. Lange[3], R.L. Savoy[4], J.R. Anderson[1], J.J. Sidtis[2], L.K. Hansen[5],
P.A. Bandettini[4], K. O'Craven[4], M. Rezza[4], B.R. Rosen[4], D.A. Rottenberg[1,2]

[1]Veterans Affairs Medical Center (VAMC) and [2]University of Minnesota, Minneapolis, USA
[3]National Institutes of Health, Bethesda; [4]Massacheusets General Hospital NMR (MGH-NMR)
Center, Boston, USA; [5]Technical University of Denmark, Lyngby, Denmark

Introduction: For normal subjects performing a left-handed sequential finger-to-thumb opposition task (1) multivariate analyses of fMRI time-series and [^{15}O]water PET scans demonstrate the existence of a statistically significant multidimensional signal structure. For standard repeated-measures experimental designs significant uncontrolled temporal effects appear as a signal dimension that is *uncorrelated* with the primary activation response for both fMRI (3 min) and PET (100 min) time scales.

Method: PET scans were acquired for three subjects at the VAMC PET Center. Each subject had four scanning sessions during a 3-6 month period ([baseline, activation, b, a, b, a, b, a]/scanning session). Scans were aligned and analyzed using the techniques described in (1) to obtain the eigenvectors from a Scaled Subprofile Model with principal component analysis (SSM/PCA). Whole-brain echo-planar fMRI scans (1.5T, 3.1 x 3.1 x 8 mm^3 voxels) were also acquired for three additional subjects at the MGH-NMR center; each subject was scanned over eight runs of 72 2.5-second scans ([24b, 24a, 24b]/run). For PET and fMRI each subject's scans were aligned and individually analyzed to obtain SSM/PCA eigenvectors (1,2) and a separate canonical variables analysis (CVA) of the eigenvectors from each subject was performed (3). CVA tested the hypothesis that each subject's group means—for 72 fMRI scans averaged across runs or 8 PET scans averaged across sessions—were identical vs. the alternative that they lay in an r-dimensional hyperplane.

Results: For PET and fMRI the CVA group means for each subject lie in a two-dimensional hyperplane (p < 0.05). Figs. 1A and 1B illustrate the time course of the 1st and 2nd canonical variates (CV's) for one of the fMRI subjects; note the hemodynamic state transitions (rise time < fall time) of CV1 and the gradual drift over time of CV2. Fig. 1C depicts the average temporal trajectory of the 72 scans/run in the "fMRI state space" defined by the CV's in Figs. 1A & 1B; similar state-space temporal trajectories exist for the other fMRI subjects. Fig. 1D illustrates the average temporal trajectory of the 8 scans in the "PET state space" defin-

Figure 1; Temporal changes across fMRI runs and PET scanning sessions from CVA (see text).

ed by the first two CV's for one of the PET subjects; ellipses represent 95% confidence intervals on the scan means and the % variance contributed by each CV to the state-space structure is recorded on the appropriate axis. The canonical eigenimages associated with CV1 for PET and fMRI contain the expected activated foci in contralateral sensory-motor cortex, SMA and ipsilateral cerebellum for all subjects analyzed. The second canonical eigenimages have no consistent pattern across subjects within or between PET and fMRI.
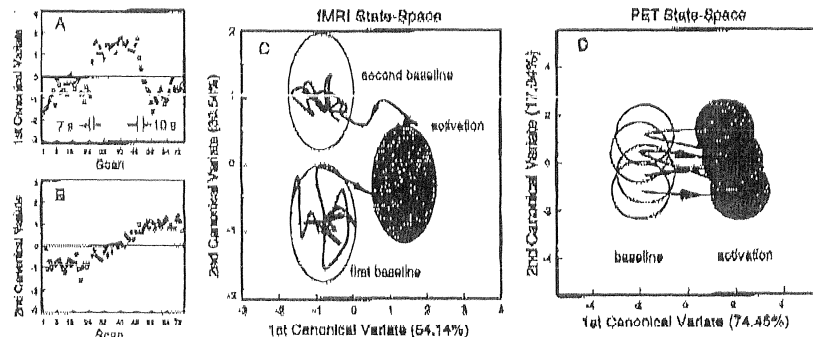
Conclusion: In sequential repeated-measures experimental designs using a simple motor task there is evidence of significant uncontrolled scan-order (temporal) effects in both PET and fMRI studies. These data suggest that repeated baseline and activation states should *not* be treated as random replicates to avoid using inflated noise variances, and that experimental designs using randomized scan order may be important in functional activation studies.

References
1. Strother SC, Anderson JR, Schaper KA, et al. J. Cereb. Blood Flow Metab., 15:738-775, 1995
2. Jiang A, Kennedy DN, Woods R, et al. Human Brain Mapp., 1996 (in press)
3. Mardia KV, Kent JT, Bibby JM. Multivariate Analysis, 1979, London, Academic Press